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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,068	09/20/2001	Hazire Oya Alpar	41577/263898	6302

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EXAMINER	
HINES, JANA A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,068	ALPAR ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 January 2006 and 17 April 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,6-10,13,26-29,30-33 and 34* is/are pending in the application.

4a) Of the above claim(s) *26-28 and 30-32* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,6-10,13,29,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 17, 2006 has been entered.

Amendment Entry

2. The amendment entered on January 19, 2006 has been entered. Claims 2-3, 5, 11-12, 14-25 have been cancelled. Claims 26-28 and 3032 have been withdrawn. Claim 1 has been amended. Claims 1, 4, 6-10, 13, 29 and 33-34 are under consideration in this office action.

Withdrawal of Rejections

3. The following objections and rejections have been withdrawn in view of applicants' amendments and arguments:

a) The objection of claims 12 and 33 under 37 CFR 1.75(c);

b) The rejection of claims 1, 4, 6-9,12-13, 29 and 33 under 35 U.S.C. 102(b) as being anticipated by Duncan et al., (WO 94/20070 published September 15, 1994);

c) The rejection of claim 10 under 35 U.S.C. 103(a) as being unpatentable over Duncan et al., (WO 94/20070 published September 15, 1994) in view of Griffin et al., (1998); and

d) The new matter rejection of claims 1, 4, 6-10, 12-13, 29 and 33 are rejected under 35 U.S.C. 112, first paragraph.

Response to Arguments

4. Applicant's arguments filed January 19, 2006 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Written Description

5. The written description rejection of claims 1, 4, 6-10, 12-13, 29 and 33-34 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reasons already of record. The rejection was on the grounds that the claims are encompass every type of vaccine and biologically active agent that generates a protective immune response in an animal when administered.

Applicants' assert that other patents have issued with claims drawn to a wide range of biologically active agents. However it is noted that the Park et al., (US Patent

6,267,987) is not drawn to biologically active agents that generate a protective immune response. Therefore, this argument is not persuasive.

Applicants' urge that they should not have to show scientific data concerning all possible antigens. However, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic, yet these examples are not disclosed by the specification. It is unquestionable claim 1 is a broad generic with respect all possible compounds encompassed by the claims. The possible structural variations are limitless. It must not be forgotten that the MPEP states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP 2163. Here, though the claims may recite functional characteristics such as the biologically active agent generating a protective immune response, the increased effect of the biologically active agent acting as an immunostimulant and how the polymeric microcapsules are obtained. However the claims lack written description because there is no disclosure of a correlation between function and structure of the compounds. Moreover, the specification lack sufficient variety of species to reflect this variance in the genus since the specification does not provide any commensurate examples.

Again, it is the examiner's position that the specification discloses that immune responses, i.e., elevated antibody levels, were generated in mice, however it is well known that merely generating an immune response does not equate to providing

protective immunity. Thus the specification fails to provide an adequate written description of a composition comprising an undisclosed biologically active agent and adjuvant that will provide protective immunity to all types of infections and diseases. This demonstration is required for the skilled artisan to be able to use the claimed vaccines for their intended purpose of preventing any type infection or disease. Without this demonstration, the skilled artisan would not be able to reasonably predict the outcome of the administration of the claimed immunostimulant compositions, i.e. would not be able to accurately predict if protective immunity has been induced. The specification fails to teach the identity a composition with the claimed characteristics. Furthermore, the specification fails to adequately disclose a description of the claimed compositions, thus a skilled artisan would be required to *de novo* locate, identify and characterize the claimed compositions and biologically active agent with the recited abilities.

Therefore applicants' arguments are not persuasive and the full breadth of the claims fails to meet the written description provision of 35 USC 112, first paragraph, thus the rejection is maintained.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1, 4, 6-9 and 33-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Duncan et al., (WO 94/20070 published September 1994) in view of Owen et al., (US Patent 5,688,761).

The claims are drawn to an immunostimulant composition comprising pharmaceutically acceptable particles selected from polymeric microcapsules or liposomes wherein the particles comprise a biologically active agent that generates a protective immune response in an animal to which it is administered; in combination with an adjuvant chemical which increases the effect of the biologically active agent by acting as an immunostimulant, said adjuvant chemical being a positively charged cationic block copolymer or a positively charged cationic surfactant. The dependant claims are drawn to specifics about the adjuvant, particles or microcapsules.

Duncan et al., teach immunostimulant compositions comprising: biologically active agents, such as immunogens or antigens (pages 4-5, para.1). Furthermore, the composition comprises an acceptable carrier such as a mucoadhesive (page 6, para.1). Duncan et al., teach the use of mucoadhesives as adjuvants and the mixtures of the mucoadhesives can be employed (page 8, para. 1). Thus the art teaches employing at least a second adjuvant, just as required by the claims. The composition also comprises an adjuvant chemical having adjuvant properties wherein the adjuvants include block copolymers, polycations such as DEAE-4 dextran and polyarnithine (pages 9-10, para. 1). Both the polycations and the dextran are known to be polycationic substances. Duncan et al., teach the use of a variety of surfactant which are known to act as wetting agents that lower the surface tension of a liquid, allowing easier spreading, and lower

the interfacial tension between two liquids, see pages 10-11. The art teaches administration to be mucosal surfaces using different well-known modes of administration (page 10, para. 3). The compositions can also contain additional pharmaceutically acceptable excipients or core materials. Duncan et al., further teach that an enhancement in the immune response is observed when the adjuvant is combined with the immunogen and mucoadhesive (pages 10-11, para.2). The antigens are more immunogenic when they are incorporated into the polymeric microparticles, nanoparticles or liposomes (page 2, para.4). The art teaches coating and subcoating the dosage unit by conventional means (pages 11-12, para. 4-1). Thereby meeting the limitations of the claims instantly recited. However Duncan et al., do not specifically recite the use of adjuvants wherein the chemical is a positively charged cationic block copolymer or a positively charged cationic surfactant.

Owen et al., teach highly stable microemulsion formulations containing biologically or therapeutically active materials (col. 3, lines 8-12). The compositions also comprise adjuvants, stabilizers, coloring agents oils and the like (col. 5, lines 37-39). Owen et al., teach that it is well understood in the art that the nature of the oils and surfactants is not critical beyond them being pharmaceutically acceptable (col. 6, lines 60-65). Suitable cationic surfactants include cetyldimethylethylammonium bromide, cetylpyridinium chloride and other salts of these surfactants (col. 7, lines 63-65). These compositions can be administrated to mucous membranes (col. 14, lines 37-41). The capsule or tablet forms of the composition can be enterically coated by techniques well known in the art (col. 14, lines 64-68). The enteric coating solution contains polymeric

coating substances prepared using commercially available high molecular weight polymer cellulose acetate phthalate or cellulose acetate trimellitate (col. 15, lines 10-15).

Therefore, it would have been prima facie obvious at the time of applicants' invention to have used the known immunostimulant compositon as taught by Duncan et al., and modify the compositions to include a positively charged cationic surfactant in a microparticle formulation as taught by Owen et al. One would have a reasonable expectation of success in having compositions, which contain biologically active antigens, adjuvants and other polycationic substances, to further include positively charged cationic surfactants which are known in the art to be included in such formulations. Moreover, no more than routine skill would have been required to the exchange particular surfactants used in well known composition since the modification merely incorporates exchanging surfactant when other surfactants were already known in the art to act as wetting agents that lower the surface tension of a liquid, allowing easier spreading, and lower the interfacial tension between two liquids.

7. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Duncan et al., (WO 94/20070 published September 1994) and Owen et al., (US Patent 5,688,761) further view of Griffin et al., (1998).

The claims are drawn to an immunostimulant composition further comprising microcapsules which comprise poly-(L-lactide). Duncan et al., and Owen et al., have

been previously discussed however neither teaches microcapsules comprising poly-(L-lactide).

Griffin, et al. teach microencapsulation of V antigen (a biologically active agent) with poly(L)lactide which has a molecular weight of 2000 (page 517-518). Griffin et al., further teach microsphere compositions for double emulsion particles containing an aqueous solution of the V antigen of Yersinia pestis. The high molecular weight polymer is prepared in co-encapsulated preparations that also contain a pharmaceutically acceptable carrier or diluent, see Table 1 (page 518, paragraphs 1-3). Griffin et al., also teach antibody responses for microsphere compositions administered to animals at page 519-520 (also see Material and Methods and Figures I -2). Thereby teaching the immunostimulant properties of the compositions, just as required by the claims.

Therefore, it would have been prima facie obvious at the time of applicants' invention to have used the known immunostimulant compositon as taught by Duncan et al., and Owen et al., wherein the modifiation is to include poly-(L-lactide) in a microparticle formulation as taught by Griffin et al. One would have a reasonable expectation of success in having the immunostimulant composition, a muchoadhesive which already has well known properties such as low cost, high biocompatible, being biodegradable, easy chemical modification, having gel-forming properties and being useful in microspheres systems and combining it with antigens and cationic pluronic adjuvants in particle formation to achieve enhanced mucosal absorption. Moreover, no more than routine skill would have been required to the modify the well known

composition since the modification merely incorporates using antigenic and adjuvant material within microparticulate polymeric carriers to enhance adsorption.

Prior Art

8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Haga et al., (EP 595,188) teach producing vaccines using cationic surface active agents. Illum (WO 90/09780) teach drug delivery compositions comprising polycationic substances.

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines

June 15, 2006

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